

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. A method for determining whether an agent possesses a defined biological activity, the method comprising the steps of:

(a) making at least one comparison from the group consisting of:

(1) comparing an efficacy value of the agent to at least one reference efficacy value to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins;

(2) comparing a toxicity value of the agent to at least one reference toxicity value to yield a toxicity comparison result, wherein each toxicity value represents at least one expression pattern of the same toxicity-related population of genes, or at least one expression pattern of the same toxicity-related population of proteins;

(3) comparing a classifier value of the agent to at least one reference classifier value to yield a classifier comparison result, wherein each classifier value represents at least one expression pattern of the same classifier population of genes, or at least one expression pattern of the same classifier population of proteins; and

(b) using the comparison result(s) obtained in step (a) to determine whether the agent possesses the defined biological activity.

2. The method of Claim 1 comprising the steps of:

(a) making at least two comparisons from the group consisting of:

(1) comparing an efficacy value of the agent to at least one reference efficacy value to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins;

(2) comparing a toxicity value of the agent to at least one reference toxicity value to yield a toxicity comparison result, wherein each toxicity value represents at least one expression pattern of the same toxicity-related population of genes, or at least one expression pattern of the same toxicity-related population of proteins;

(3) comparing a classifier value of the agent to at least one reference classifier value to yield a classifier comparison result, wherein each classifier value represents at least one expression pattern of the same classifier population of genes, or at least one expression pattern of the same classifier population of proteins; and

(b) using the comparison results obtained in step (a) to determine whether the agent possesses the defined biological activity.

3. The method of Claim 1 comprising the steps of:

(a) comparing an efficacy value of the agent to at least one reference efficacy value to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins;

(b) comparing a toxicity value of the agent to at least one reference toxicity value to yield a toxicity comparison result, wherein each toxicity value represents at least one expression pattern of the same toxicity-related population of genes, or at least one expression pattern of the same toxicity-related population of proteins;

(c) comparing a classifier value of the agent to at least one reference classifier value to yield a classifier comparison result, wherein each classifier value represents at least one expression pattern of the same classifier population of genes, or at least one expression pattern of the same classifier population of proteins; and

(d) using the efficacy comparison result, the toxicity comparison result and the classifier comparison result to determine whether the agent possesses the defined biological activity, wherein steps (a), (b) and (c) can occur in any order with respect to each other.

4. The method of Claim 1 wherein the agent is a chemical agent.

5. The method of Claim 1 wherein the defined biological activity is stimulation of a biological response.

6. The method of Claim 1 wherein the defined biological activity is inhibition of a biological response.

7. The method of Claim 1 wherein the defined biological activity is amelioration of at least one symptom of a disease in a mammal.

8. The method of Claim 1 wherein the defined biological activity is partial agonist activity with respect to a biological response, or with respect to a protein that mediates a biological response.

9. The method of Claim 8 wherein the defined biological activity is partial agonist activity with respect to PPAR γ .

10. The method of Claim 1 wherein the at least one reference efficacy value is the efficacy value of a reference agent that possesses the defined biological activity.

11. The method of Claim 1 wherein the at least one reference toxicity value is the toxicity value of a reference agent that possesses the defined biological activity.

12. The method of Claim 1 wherein the at least one reference classifier value is the classifier value of a reference agent that possesses the defined biological activity.

13. The method of Claim 1 wherein at least one member of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent is calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in living cells cultured *in vitro*.

14. The method of Claim 13 wherein at least two members of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in living cells cultured *in vitro*.

15. The method of Claim 13 wherein the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in living cells cultured *in vitro*.

16. The method of Claim 13 wherein the living cells are selected from the group consisting of heart cells, liver cells and adipocyte cells.

17. The method of Claim 16 wherein the living cells are 3T3L1 adipocyte cells.

18. The method of Claim 1 wherein the defined biological activity is the ability to affect a biological process *in vivo*, and wherein at least one member of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent is calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in living cells cultured *in vitro*.

19. The method of Claim 18 wherein the biological process is an acute or chronic disease in a mammal.

20. The method of Claim 1 wherein the defined biological activity is the ability to affect a biological process *in vivo*, and wherein at least two members of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in living cells cultured *in vitro*.

21. The method of Claim 20 wherein the biological process is an acute or chronic disease in a mammal.

22. The method of Claim 1 wherein the defined biological activity is the ability to affect a biological process *in vivo*, and wherein the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in living cells cultured *in vitro*.

23. The method of Claim 22 wherein the biological process is an acute or chronic disease in a mammal.

24. The method of Claim 1 wherein the defined biological activity is the ability to affect a biological process in a first living tissue, and wherein at least one member of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent is calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in a second living tissue, wherein the first living tissue is a different type of tissue than the second living tissue.

25. The method of Claim 1 wherein the defined biological activity is the ability to affect a biological process in a first living tissue, and wherein at least two members of the group consisting of the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in a second living tissue, wherein the first living tissue is a different type of tissue from the second living tissue.

26. The method of Claim 1 wherein the defined biological activity is the ability to affect a biological process in a first living tissue, and wherein the efficacy value of the agent, the toxicity value of the agent and the classifier value of the agent are calculated from at least one member of the group consisting of gene expression levels and protein expression levels measured in a second living tissue, wherein the first living tissue is a different type of tissue than the second living tissue.

27. The method of Claim 1 wherein at least one member of the group consisting of the efficacy-related population of genes and the efficacy-related population of proteins yields at least one efficacy-related gene expression pattern, or efficacy-related protein expression pattern, in response to the agent, that correlates with the presence of at least one desired biological response caused by the agent in a living thing, wherein the at least one efficacy-related gene expression pattern, or at least one efficacy-related protein expression pattern, appears before the desired biological response.

28. The method of Claim 1 wherein at least one member of the group consisting of the toxicity-related population of genes and the toxicity-related population of proteins yields at least one toxicity-related gene expression pattern, or toxicity-related

protein expression pattern, in response to the agent, that correlates with the presence of at least one undesirable biological response caused by the agent in a living thing, wherein the at least one toxicity-related gene expression pattern, or at least one toxicity-related protein expression pattern, appears before the undesirable biological response.

29. The method of Claim 1 wherein (1) at least one member of the group consisting of the efficacy-related population of genes and the efficacy-related population of proteins yields at least one efficacy-related gene expression pattern, or efficacy-related protein expression pattern, in response to the agent, that correlates with the presence of at least one desired biological response caused by the agent in a living thing, wherein the at least one efficacy-related gene expression pattern, or at least one efficacy-related protein expression pattern, appears before the desired biological response; and (2) at least one member of the group consisting of the toxicity-related population of genes and the toxicity-related population of proteins yields at least one toxicity-related gene expression pattern, or at least one toxicity-related protein expression pattern, in response to the agent, that correlates with the presence of at least one undesirable biological response caused by the agent in a living thing, wherein the at least one toxicity-related gene expression pattern, or at least one toxicity-related protein expression pattern, appears before the undesirable biological response.

30. The method of Claim 1 comprising the steps of:

(a) making at least one comparison from the group consisting of:

(1) comparing an efficacy value of the agent to a scale of efficacy values to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins;

(2) comparing a toxicity value of the agent to a scale of toxicity values to yield a toxicity comparison result, wherein each toxicity value represents at least one expression pattern of the same toxicity-related population of genes, or at least one expression pattern of the same toxicity-related population of proteins;

(3) comparing a classifier value of the agent to a scale of classifier values to yield a classifier comparison result, wherein each classifier value represents at least

one expression pattern of the same classifier population of genes, or at least one expression pattern of the same classifier population of proteins; and

(b) using the comparison result(s) obtained in step (a) to determine whether the agent possesses the defined biological activity.

31. The method of Claim 30 comprising the steps of:

(a) making at least two comparisons from the group consisting of:

(1) comparing an efficacy value of the agent to a scale of efficacy values to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins;

(2) comparing a toxicity value of the agent to a scale of toxicity values to yield a toxicity comparison result, wherein each toxicity value represents at least one expression pattern of the same toxicity-related population of genes, or at least one expression pattern of the same toxicity-related population of proteins;

(3) comparing a classifier value of the agent to a scale of classifier values to yield a classifier comparison result, wherein each classifier value represents at least one expression pattern of the same classifier population of genes, or at least one expression pattern of the same classifier population of proteins; and

(b) using the comparison results obtained in step (a) to determine whether the agent possesses the defined biological activity.

32. The method of Claim 30 comprising the steps of:

(a) comparing an efficacy value of the agent to a scale of efficacy values to yield an efficacy comparison result, wherein each efficacy value represents at least one expression pattern of the same efficacy-related population of genes, or at least one expression pattern of the same efficacy-related population of proteins;

(b) comparing a toxicity value of the agent to a scale of toxicity values to yield a toxicity comparison result, wherein each toxicity value represents at least one expression pattern of the same toxicity-related population of genes, or at least one expression pattern of the same toxicity-related population of proteins;

(c) comparing a classifier value of the agent to a scale of classifier values to yield a classifier comparison result, wherein each classifier value represents at least one

expression pattern of the same classifier population of genes, or at least one expression pattern of the same classifier population of proteins; and

(d) using the efficacy comparison result, the toxicity comparison result and the classifier comparison result to determine whether the agent possesses the defined biological activity, wherein steps (a), (b) and (c) can occur in any order with respect to each other.

33. A population of oligonucleotide probes selected from the group consisting of the population of oligonucleotide probes set forth in Table 1 (SEQ ID NOs: 51-102), the population of oligonucleotide probes set forth in Table 2 (SEQ ID NOs: 52, 53, 58, 59, 65, 66, 68, 69, 71, 73, 75, 76, 78, 82, 86, 88-90, 93, 94, 96, 101), the population of oligonucleotide probes set forth in Table 4 (SEQ ID NOs: 153-207), the population of oligonucleotide probes set forth in Table 5 (SEQ ID NOs: 213-218), the population of oligonucleotide probes set forth in Table 6 (SEQ ID NOs: 551-894, 155, 157, 164, 171, 178, 179, 185, 188, 204-206), the population of oligonucleotide probes set forth in Table 7 (SEQ ID NOs: 950-1019, 863, 93, 94, 97), the population of oligonucleotide probes set forth in Table 8 (SEQ ID NOs: 1036-1057, 951, 955, 957, 863, 959, 960, 63, 962, 966, 971-974, 980, 981, 984, 987, 989, 991-996, 93, 94, 998-1001, 97, 1004-1014, 1017-1019), the population of oligonucleotide probes set forth in Table 9 (SEQ ID NOs: 1239-1428, 558, 561, 158, 565, 574, 576, 578, 585, 592, 597, 600, 609, 612, 613, 617, 163, 625, 641-643, 646, 647, 655-657, 661, 666, 171, 681, 697, 700, 706, 707, 712, 720, 727, 740, 745, 748, 749, 755-757, 762, 766, 767, 769-771, 773, 778, 780, 786, 789, 794, 800, 803, 804, 188, 189, 191, 813, 814, 822, 823, 556, 828, 831, 832, 836, 840, 844, 864, 871, 876, 878, 883, 884, 889-891), the population of oligonucleotide probes set forth in Table 10 (SEQ ID NOs: 1449-1471, 952, 956, 957, 963, 975, 976, 981, 983, 984, 986, 990, 999-1001, 1004-1007, 1012-1014), the population of oligonucleotide probes set forth in Table 12 (SEQ ID NOs: 1731-1996, 52, 951, 1450, 957, 1452, 1455, 65, 68, 69, 72, 75, 1457, 967, 1458, 970, 971, 974, 1462, 82, 977, 978, 982, 90, 989, 990, 215, 999-1001, 96, 1468, 1005, 1006, 218, 1014, 1018, 1019), and the population of oligonucleotide probes set forth in Table 14 (SEQ ID NOs: 2796-3683, 1732, 1734, 53, 1740, 1449, 1450, 1747, 1748, 1037, 1759, 957, 1774, 60, 1780, 63, 1797, 962, 1808, 1041, 1809, 1817, 1818, 1820, 1824, 71, 72, 1833, 966, 1873, 970-973, 1879, 1046, 1047, 976, 1898, 1904, 80, 1910, 86, 1932, 1933, 1941, 1049, 989, 1953, 991-993, 1050,

1051, 994, 215, 216, 93, 94, 998-1001, 1465-1467, 1957, 1002, 214, 1962, 1005-1007, 1056, 1057, 1009-1014, 1974, 1975, 1977, 1979, 1016-1019, 1994, 101).

34. A method of identifying an efficacy-related population of genes or proteins, wherein the method comprises the steps of:

(a) contacting a living thing with an agent that is known to elicit a desired biological response; and

(b) identifying an efficacy-related population of genes or proteins in the living thing that yields an expression pattern that correlates with the occurrence of the desired biological response caused by the agent.

35. The method of Claim 34 wherein the living thing is a mammal.

36. The method of Claim 34 wherein the living thing is a human being.

37. The method of Claim 34 wherein an efficacy-related population of genes is identified.

38. The method of Claim 34 wherein an efficacy-related population of proteins is identified.

39. The method of Claim 34 wherein the agent is a chemical agent.

40. The method of Claim 34 wherein an efficacy-related population of genes or proteins is identified by:

(a) measuring the level of expression of each member of a multiplicity of genes or proteins in the living thing, contacted with the agent, to yield a multiplicity of expression values;

(b) measuring the level of expression of each member of the same multiplicity of genes or proteins in a reference living thing, that is not contacted with the agent, to yield a multiplicity of reference expression values; and

(c) comparing the multiplicity of expression values with the multiplicity of reference expression values to identify an efficacy-related population of genes or proteins, wherein each individual gene or protein has an expression value in response to the agent that is significantly different from the corresponding reference expression value.

41. The method of Claim 34 wherein the expression pattern of the efficacy-related population of genes or proteins appears in the living thing before the occurrence of the desired biological response caused by the agent.

42. The method of Claim 34 wherein the desired biological response does not occur in the living thing.

43. The method of Claim 42 wherein the living thing consists essentially of epididymal white adipose tissue.

44. The method of Claim 34 wherein the living thing suffers from a disease and the desired biological response is amelioration of at least one symptom of the disease.

45. The method of Claim 44 wherein the living thing is a mammal, and the disease is selected from the group consisting of type II diabetes, hypercholesterolemia, cancer, inflammation, obesity, schizophrenia and Alzheimer's disease.

46. The method of Claim 34 further comprising:

(a) contacting the living thing with an agent that is known to elicit at least two different desired biological responses in the living thing, wherein elicitation of a first desired biological response is mediated by a first target molecule, and elicitation of a second desired biological response is mediated by a second target molecule that is different from the first target molecule;

(b) identifying an efficacy-related population of genes or proteins that yields an expression pattern that correlates with the occurrence of the first and second desired biological responses in response to the agent;

(c) contacting a modified living thing with the agent, wherein the modified living thing is a member of the same species as the living thing and does not include any functional first target molecules;

(d) identifying an efficacy-related population of genes or proteins that yields an expression pattern that correlates with the occurrence of the second desired biological response in the modified living thing in response to the agent; and

(e) comparing the efficacy-related population of genes or proteins identified in step (b) with the efficacy-related population of genes or proteins identified in step (d)

to identify an efficacy-related population of genes or proteins that yields an expression pattern that correlates with the occurrence of the first desired biological response caused by the agent.

47. The method of Claim 46 wherein the first target molecule is a PPAR α receptor and the second target molecule is a PPAR γ receptor.

48. The method of Claim 46 wherein the first target molecule is a PPAR γ receptor and the second target molecule is a PPAR α receptor.

49. A method of identifying a toxicity-related population of genes or proteins, wherein the method comprises the steps of:

(a) contacting a living thing with an agent that is known to elicit an undesirable biological response; and

(b) identifying a toxicity-related population of genes or proteins that yields an expression pattern that correlates with the occurrence of the undesirable biological response caused by the agent.

50. The method of Claim 49 wherein the living thing is a mammal.

51. The method of Claim 49 wherein the living thing is a human being.

52. The method of Claim 49 wherein a toxicity-related population of genes is identified.

53. The method of Claim 49 wherein a toxicity-related population of proteins is identified.

54. The method of Claim 49 wherein the agent is a chemical agent.

55. The method of Claim 49 wherein a toxicity-related population of genes or proteins is identified by:

(a) measuring the level of expression of each member of a multiplicity of genes or proteins in the living thing, contacted with the agent, to yield a multiplicity of expression values;

(b) measuring the level of expression of each member of the same multiplicity of genes or proteins in a reference living thing, that is not contacted with the agent, to yield a multiplicity of reference expression values; and

(c) comparing the multiplicity of expression values with the multiplicity of reference expression values to identify a toxicity-related population of genes or proteins, wherein each individual gene or protein has an expression value in response to the agent that is significantly different from the corresponding reference expression value.

56. The method of Claim 49 wherein the expression pattern of the toxicity-related population of genes or proteins appears in the living thing before the occurrence of the undesirable biological response in response to the agent.

57. The method of Claim 49 wherein the undesirable biological response does not occur in the living thing.

58. The method of Claim 49 wherein the living thing consists essentially of epididymal white adipose tissue.

59. The method of Claim 49 wherein the undesirable biological response is selected from the group consisting of increased blood plasma volume, increased heart size, increased blood glucose concentration and increased total cholesterol.

60. The method of Claim 49 further comprising:

(a) contacting a living thing with an agent that is known to elicit a desirable biological response and an undesirable biological response in the living thing, wherein elicitation of the desirable biological response is mediated by a first target molecule, and elicitation of the undesirable biological response is mediated by a second target molecule;

(b) identifying a population of genes or proteins that yields an expression pattern that correlates with the occurrence of the desirable and undesirable biological responses caused by the agent;

(c) contacting a modified living thing with the agent, wherein the modified living thing is a member of the same species as the living thing and does not include any functional second target molecules;

(d) identifying an efficacy-related population of genes or proteins that yields an expression pattern that correlates with the occurrence of the desirable biological response caused by the agent; and

(e) comparing the population of genes or proteins identified in step (b) with the efficacy-related population of genes or proteins identified in step (d) to identify a toxicity-related population of genes or proteins that yields an expression pattern that correlates with the occurrence of the undesirable biological response caused by the agent.

61. The method of Claim 60 wherein the first target molecule is a PPAR γ receptor and the second target molecule is a PPAR α receptor.

62. A method for identifying a classifier population of genes or proteins, wherein the method comprises the steps of:

(a) contacting a living thing with a first reference agent that is known to cause a first biological response;

(b) identifying a first population of genes or proteins that yields an expression pattern that correlates with the occurrence of the first biological response caused by the first reference agent;

(c) contacting a living thing with a second reference agent that is known to cause a second biological response, wherein the living thing is the same living thing that is contacted with the first reference agent, or is a different living thing that is a member of the same species as the living thing that is contacted with the first reference agent;

(d) identifying a second population of genes or proteins that yields an expression pattern that correlates with the occurrence of the second biological response caused by the second reference agent; and

(e) comparing the first population of genes or proteins to the second population of genes or proteins and thereby identifying a classifier population of genes or proteins that produces an expression pattern that most clearly distinguishes between the first reference agent and the second reference agent.

63. The method of Claim 62 wherein the living thing is a mammal.

64. The method of Claim 62 wherein the living thing is a human being.

- 65. The method of Claim 62 wherein a classifier population of genes is identified.
- 66. The method of Claim 62 wherein a classifier population of proteins is identified.
- 67. The method of Claim 62 wherein the agent is a chemical agent.